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Formulation, Optimization, and Evaluation of Herbal (*Nelumbo nucifera*) Anti-inflammatory Gel for Topical Application

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ABSTRACT

The gels have the safest, easily applicable and most effective due to its directly applicable to the infected part of the skin with minimal adverse effect. This research explores the development and characterisation of an anti-inflammatory gel using lotus stem, a plant that has long been valued for its therapeutic qualities, especially its ability to reduce inflammation. Dried ethanolic extract of lotus stem was carefully blended with essential components like Carbopol 934, propylene glycol 400, methylparaben, propylparaben, and distilled water in precisely the right amounts to create the gel formulation. Triethanolamine was gradually added in order to maintain the ideal pH range (6.8–7.0) for skin compatibility. The developed product was subjected to extensive testing, which included analyses of its physical characteristics, pH, spreadability, viscosity, homogeneity, and potential for skin irritation in animal models. The results highlighted the gel's positive qualities, such as visually-pleasing look, even dispersion, and effective spreadability, indicating bright futures for its use in anti-inflammatory treatment.

Keywords: Herbal anti-inflammatory gel; *Nelumbo nucifera*; Skin; Development; Characterisation; Therapeutic qualities; Spreadability; Viscosity; Homogeneity; Potential for skin irritation.

1. Introduction

1.1. An Overview of Gels

Traditional medicine and conventional medicine play a major role in health service around the globe. The herbal medicine is still the mainstay of about 75–80% of the world's population, mainly in developing countries. Herbal drugs and medicines consist of plant and its parts to treat illness, injuries, and diseases and promote healing. Gels are new form of medicine in order to achieve greater therapeutic efficacy and higher patient compliance. Direct applicable to the damage or disease part without going to the first pass metabolism and less side effect [1]-[4].

1.2. Mechanism of gel penetration into the skin

It involves a combination of process, primarily driven by the properties of the gel and skin. Here are the key factors:

1.2.1. Diffusion

The drug molecules in the gel move from an area of higher concentration (the gel) to lower concentration (the skin). This process occurs through the skin's outer layer, the stratum corneum.

1.2.2. Solubility

The drug in the gel needs to be soluble in both the gel matrix and the skin to facilitate penetration. This is crucial for effective diffusion through the skin layers.

1.2.3. Size of Molecules

Smaller drug molecules generally penetrate the skin more easily. The gel formulation should allow for the optimal size of drug particles for efficient skin absorption.

1.2.4. Enhancers

Some gel formulations include chemical enhancers that temporarily alter the structure of the stratum corneum, facilitating better penetration of the drug.

1.2.5. Hydration of Skin

Gels may hydrate the skin, temporarily reducing the barrier function of the stratum corneum and enhancing drug penetration.

1.2.6. Temperature

Higher temperatures can increase skin permeability, aiding the penetration of the drug from the gel.

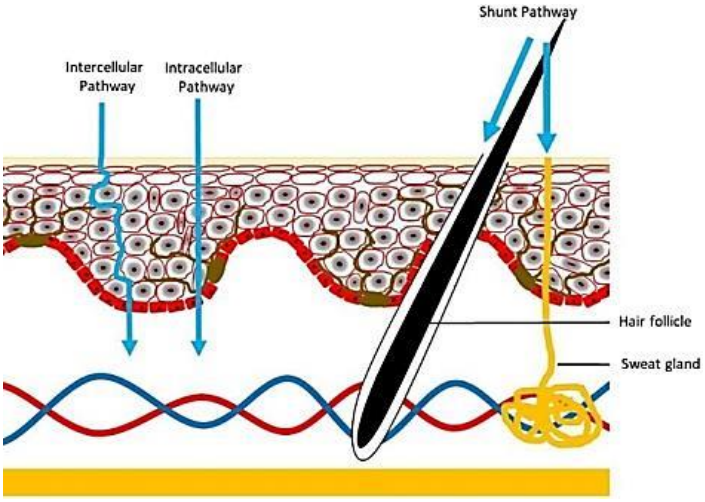

Figure 1. Skin Penetration of gel [2]

1.3. Study Objectives

The following are the main objectives of this study: (1) Formulate a gel containing *Nelumbo nucifera* extract as the active ingredient. (2) Optimize the formulation parameters to enhance the stability. (3) Formulating the pH of the gel. (4) Evaluate the viscosity of the gel. (5) Determining the spreadability and extrudability of the gel.

2. Method of preparation of gel

2.1. Preparation of ethanolic extracts

Stem of *Nelumbo nucifera* were collected from Gwalior region Stem of *Nelumbo nucifera* were dried under shade after cutting into small pieces and then coarsely powdered with a mechanical grinder. The powder was passed through sieve No. 40 and extracted with ethanol as solvent in Soxhlet extractor. The resulting extracts were cooled and filtered. The filtrate was evaporated in vacuum to give a residue [5].

2.2. Formulation of topical gel

Using a mechanical stirrer, 1% w/w concentration of gelling agent Carbopol 934 was combined with deionized water to create an herbal gel. After that, tri-ethanolamine was added drop-wise while stirring continuously to maintain the skin's pH of 6.8–7. Different amounts of both extracts—0.15,0.2,0.25,0.3, and 0.35% w/w—were

added to the gel and agitated for a long enough period of time to ensure that the extract was evenly mixed throughout the gel base. To fill the produced gel, collapsible tubes were utilised. These mixtures were kept in a dry, cool environment. The formulation was assessed based on the subsequent parameters [7].

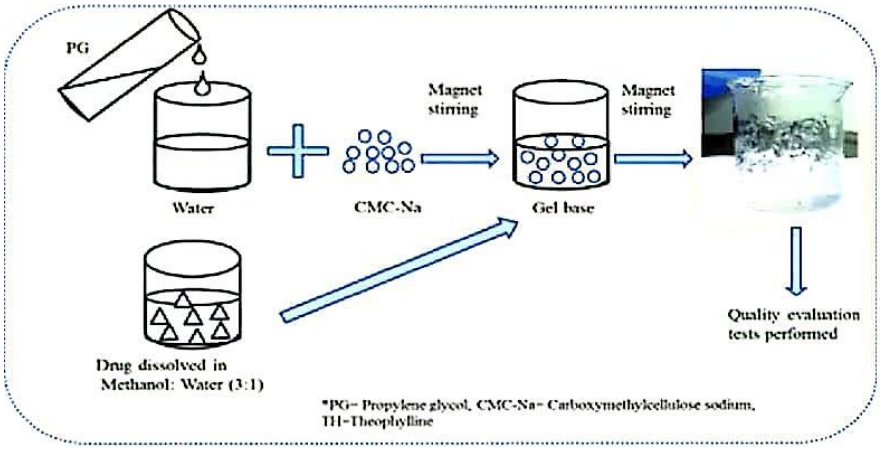

Figure 2. Preparation of Gel [7]

2.3. Physical Properties

Apart from assessing physicochemical characteristics such as colour, smell, and homogeneity in the gel compositions, additional critical elements were examined to guarantee product effectiveness and quality. These included examinations of the gel's viscosity to ascertain its thickness and flow features, analyses of its texture to comprehend its tactile qualities, and pH level evaluations to determine the gel's acidity or alkalinity. Such thorough analyses assist in adjusting formulations to satisfy intended criteria and user preferences [8].

2.4. Stability study

The prepared gels were divided into three groups. These three gel formulation groups were stored at a and put into collapsible aluminum tubes. (i) The room's temperature is 25 °C; (ii) 40 °C; and (iii) 4 °C.

The gel formulation was stored for three months. Samples were removed every month for three months, and the amount of drugs in them was assessed. At the end of the third month, their physical characteristics and product integrity were evaluated.

Physical evaluation – The product's nature, extrudability, pH, viscosity, leak, and phase separation were among the physical parameters that were considered for the evaluation [9].

2.5. pH Measurements

The pH measurements of the gel were carried out using a digital pH meter by dipping the glass electrode completely into the gel system so as to cover the electrode [4].

2.6. Determination of viscosity

Viscosities of the gel were determined by using Brookfield viscometer. Spindle type, RV-7 at 20 rpm. 100 gm of the gel was taken in a beaker and the spindle was dipped in it and rotated for about 5 minutes and then reading was taken [10].

2.7. Extrudability

Measuring the force needed to extrude the material from the tube is a helpful empirical test. The formulations were put into collapsible metal tubes with a 5 mm nasal tip whole. The quantity of gel that extruded from the tip of the tube when pressure was applied was used to measure the extrudability of the tube. The formulation's extrudability was examined, and the outcomes were recorded [11].

2.8. Spreadability

Standard-sized glass slides were taken in two sets. The mixture of herbal gel was applied on top of one of the presentation slides. The gel was positioned between the two slides in a region that was occupied by a distance of 7.5 cm along the slides when the second slide was positioned on top of the gel. Gel weighing one hundred grams was applied on the upper slides, and the gel between the two slides was uniformly compressed to create a thin layer. After removing the weight, the extra gel that was sticking to the slides was scraped off. The two slides were positioned so that only the upper slides could come loose from their fixed position on a stand without the least disturbance off freely by the weight's force binding it. Carefully, weight was fastened to the upper slide. The amount of time it took for the top slide to split and move beneath the weight's influence, away from the bottom slide was observed. Three iterations of the experiment were conducted, and the mean time was calculated [12].

The formula for calculating spreadability was $S = m \times l/t$ (1)

3. Results and Discussion

The herbal gel was made with the constituent combinations indicated in Table 1 and put through a number of parameter evaluations. Using a Brookfield viscometer, the prepared gel's viscosity was measured. The ideal viscosity was identified in each of these formulations, and the outcomes are displayed in Table 2. In order for the gel to be applied and accepted by the patient, it must be extruded from the tube. Gels with a high consistency might not extrude from the tube, whereas gels with a low viscosity might flow out of the tube fast; therefore, the gel needs to have the right consistency to extrude from the tube. All gel formulations were determined to have good extrudability; the spreadability shown in table no.3. All developed formulations had pH values between 6-7, which is deemed adequate to reduce the possibility of skin irritation upon application table no.4 shown the pH value. When they were first created, none of the formulations had any fine particles, and they all remained homogenous after three months, when the stability test was conducted. Furthermore, the preparation was stable under typical storage settings, according to the stability study's findings. Stability study is shown in Table 5.

Table 1. Composition of Gel formulation

Ingredient	**F1**	**F2**	**F3**	**F4**	**F5**
Extract	0.15	0.2	0.25	0.3	0.35
Carbopol 934	1	1	1	1	1
Methyl Paraben	0.2	0.2	0.2	0.2	0.2
Propyl Paraben	0.1	0.1	0.1	0.1	0.1

Propylene Glycol	5	5	5	5	5
Triethanolamine	q.s	q.s	q.s	q.s	q.s

The results were shown in Table below.

Table 2. Viscosity of gel formulations

S. No.	Formulation	Viscosity
1	F1	36030
2	F2	41008
3	F3	36030
4	F4	51020
5	F5	32090

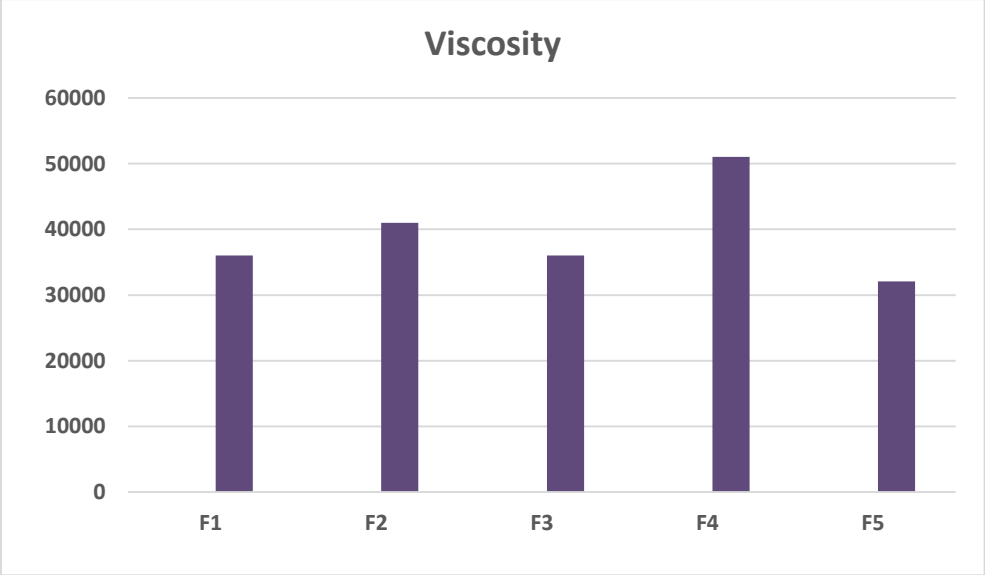

Figure 3. Viscosity

Table 3. Spreadability of gel formulations

S. No.	Formulation	Time taken (minutes)	Spreadability
1	F1	30	8.1
2	F2	30	7.7
3	F3	30	7.5
4	F4	30	7.6
5	F5	30	7.8

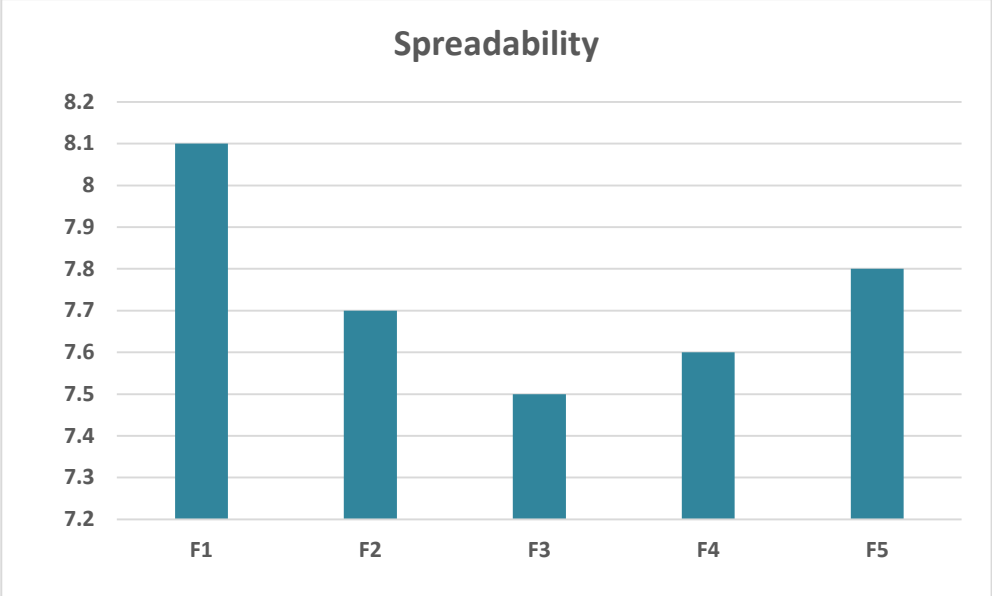

Figure 4. Spreadability

Table 4. pH of gel formulation

S. No.	Formulation	pH
1	F1	7.0
2	F2	6.7
3	F3	6.8
4	F4	6.4
5	F5	6.3

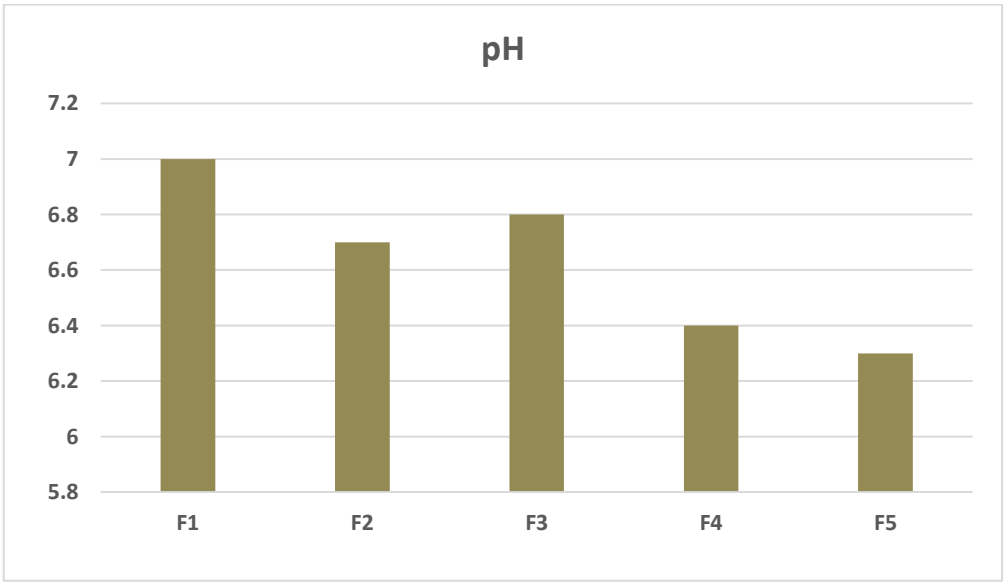

Figure 5. pH

Gel formulation stability tests were conducted at room temperature, 40 °C, and refrigerator temperature (4 °C). Physical assessment of the produced gel is displayed in the Table.

Table 5. Stability Study

Parameter	**Room Temperature (25 °C)**	**40 ^{0}C**	**4 ^{0}C**
Visual Appearance			
• Initial	Brownish green colour gel	Brownish green colour gel	Brownish green colour gel
• 1 month	Brownish green colour gel	Brownish green colour gel	Brownish green colour gel
• 2 month	Brownish green colour gel	Brownish green colour gel	Brownish green colour gel
• 3 month	Brownish green colour gel	Brownish green colour gel	Brownish green colour gel
pH			
• Initial	7.0	7.0	7.0
• 1 month	6.7	6.7	6.7
• 2 month	6.8	6.8	6.8
• 3 month	6.4	6.4	6.4
Viscosity			
• Initial	36030	36030	36030
• 1 month	41008	41008	41008
• 2 month	36030	36030	36030
• 3 month	51020	51020	51020
Extrudability			
• Initial	Satisfactory	Satisfactory	Satisfactory
• 1 month	Satisfactory	Satisfactory	Satisfactory
• 2 month	Satisfactory	Satisfactory	Satisfactory
• 3 month	Satisfactory	Satisfactory	Satisfactory
Phase Separation			
• Initial	Not found	Not found	Not found
• 1 month	Not found	Not found	Not found
• 2 month	Not found	Not found	Not found
• 3 month	Not found	Not found	Not found

Texture			
• Initial	Smooth	Smooth	Smooth
• 1 month	Smooth	Smooth	Smooth
• 2 month	Smooth	Smooth	Smooth
• 3 month	Smooth	Smooth	Smooth

4. Conclusion

Gels present a promising solution for addressing discomfort and swelling associated with various conditions. Gels are seen as effective remedies for alleviating discomfort and swelling related to different ailments. Their lightweight texture, easy absorption, and customizable formulation make them a popular choice for consumers seeking quick and effective results. Gels are favored by consumers because they are light, absorb easily, and can be tailored to specific needs, providing fast and efficient relief. The gel gives a cooling sensation after application to the skin. Upon application, the gel creates a cooling effect on the skin, offering additional comfort. Evaluation, including testing for safety and skin compatibility, ensures that the gel meets quality standards and provides reliable relief without adverse effects. Rigorous evaluation, which includes safety and skin compatibility tests, guarantees that the gel complies with quality benchmarks and delivers consistent relief without causing any negative effects.

5. Future Suggestions

(1) Nanotechnology Integration: Investigate the potential benefits of incorporating nanotechnology into the gel formulation to enhance the delivery of active compounds, improve skin penetration, and increase bioavailability, thereby maximizing the anti-inflammatory effects.

(2) Synergistic Herbal Combinations: Explore the synergistic effects of combining *Nelumbo nucifera* extract with other herbal extracts known for their anti-inflammatory properties, such as turmeric (*Curcuma longa*) or aloe vera, to create a more potent and versatile anti-inflammatory gel formulation.

(3) Enhanced Stability and Shelf-life: Conduct studies to optimize the formulation to enhance stability and prolong shelf-life, utilizing techniques such as microencapsulation or the addition of natural preservatives to prevent degradation of active compounds over time.

(4) Clinical Trials and Efficacy Studies: Conduct rigorous clinical trials to evaluate the efficacy and safety of the herbal anti-inflammatory gel in human subjects, comparing its effectiveness with existing synthetic anti-inflammatory gels or creams. This will provide valuable evidence for its clinical use and potential as an alternative to conventional treatments.

(5) Formulation Customization for Specific Conditions: Investigate the customization of the gel formulation to target specific inflammatory conditions, such as arthritis, dermatitis, or muscle strains, by adjusting the concentration of active ingredients or incorporating additional complementary ingredients tailored to the particular needs of each condition.

Declarations

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Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

All the authors took part in literature review, analysis and manuscript writing equally.

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